

From the  
INTERNATIONAL SEARCHING AUTHORITY

PCT

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

To:

see form PCT/ISA/220

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/GB2004/003935

International filing date (day/month/year)  
15.09.2004

Priority date (day/month/year)  
15.09.2003

International Patent Classification (IPC) or both national classification and IPC  
A61K9/72, A61K31/55, A61P15/00

Applicant  
VECTURA LIMITED

**1. This opinion contains indications relating to the following items:**

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

**2. FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

**3. For further details, see notes to Form PCT/ISA/220.**

Name and mailing address of the ISA:



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**Box No. I Basis of the opinion**

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1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.  
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:  
☐ a sequence listing  
☐ table(s) related to the sequence listing
  - b. format of material:  
☐ in written format  
☐ in computer readable form
  - c. time of filing/furnishing:  
☐ contained in the international application as filed.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

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**Box No. II    Priority**

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1. ☒ The following document has not been furnished:

☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. ☐ It has not been possible to consider the validity of the priority claim because a copy of the priority document was not available to the ISA at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

4. Additional observations, if necessary:

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 23,24

because:

- ☒ the said international application, or the said claims Nos. 23,24 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. -
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
  - the written form ☐ has not been furnished
  - ☐ does not comply with the standard
  - the computer readable form ☐ has not been furnished
  - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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**1. Statement**

Novelty (N)	Yes: Claims	5,6,17
	No: Claims	1-4,7-16,18-31
Inventive step (IS)	Yes: Claims	
	No: Claims	1-31
Industrial applicability (IA)	Yes: Claims	1-22,25-31
	No: Claims	

**2. Citations and explanations**

see separate sheet

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**Box No. VI Certain documents cited**

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**1. Certain published documents (Rules 43bis.1 and 70.10)**

and /or

**2. Non-written disclosures (Rules 43bis.1 and 70.9)**

see form 210

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claims 23-24 relate to subject-matter being not-patentable having regard to Rule 39.1(v) PCT. No search report has been established for the said claims and consequently no opinion will be formulated.

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Reference is made to the following document/s/:

- D1: WO 2005/004855 A (VAISMAN, JAKOV) 20 January 2005
- D2: US-B1-6 495 154 (TAM PETER ET AL) 17 December 2002
- D3: DE 195 19 056 A1 (KLINGE PHARMA GMBH) 16 January 1997
- D4: WO 02/094232 A (ALEXZA MOLECULAR DELIVERY CORP) 28 November 2002

The composition, method and use according to independent claims 1, 23 and 25 are not novel (Art.33(2) PCT) in view of prior art disclosures which can be taken from D2-D4.

D2, which is considered the closest state of the art, discloses a composition for treating premature ejaculation by pulmonary inhalation (e.g. example 5) comprising clomipramine as the active agent. Accordingly, independent claims 1, 23 and 25 are anticipated by said document.

D3 and D4 disclose antidepressant compositions for pulmonary application (cf. passages cited in the search report). Liquid formulations as well as dry powder formulations are disclosed. Accordingly, independent claim 1 is anticipated by D3 and D4.

In view of the state of the art disclosed in D2-D4, also the dependent claims 2-22, 24, 26-31 do not appear to contain any additional features which, in combination with the features of any claim to which they refer, would render the claimed subject-matter novel and/or inventive (Art.33(2)-(3) PCT).

The specific embodiments are known or at least suggested by the state of the art. The pulmonary administration of tricyclic antidepressants, such as clomipramine, is suggested and disclosed by D2. Also the combination with other therapeutic agents, such as benzodiazepines is anticipated by D2. The formulation of tricyclic antidepressants into a composition suited for pulmonary administration is also generally known in the art and e.g. illustrated by D2 (liquid composition), D3 (dry powder + liquid propellant compositions) and D4 (condensation aerosols). None of the claimed features appears to bring a solution to any specific problem, as compared to the state of the art, which solution would involve an inventive step.

The problem to be solved by the present application (cf. page 5, lines 6-19) appears to be the provision of a composition for treating premature ejaculation which has a rapid onset of the desired therapeutic effect and which is suited for "on demand" administration of low doses, such as to avoid adverse side effects. Document D2 deals with the same problem and the solution disclosed does not differ from the present application, i.e. "on demand" pulmonary inhalation of low doses of tricyclic antidepressants is taught by D2.

#### **Re Item VI**

##### **Certain documents cited**

Document D1, published after the effective date of filing of the present application, contains subject-matter (cf. passages cited in the ISR) which is considered relevant for the present application (Rule 70.10 PCT).